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Physician Practice Patterns for Performing Thoracentesis in Patients taking Anticoagulant Medications

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Abstract

Background: Patients undergoing thoracentesis often have comorbid conditions or take medications that potentially put them at higher bleeding risk. Direct oral anticoagulant (DOAC) use has also increased significantly. There are no published guidelines or consensus on when to perform thoracentesis in patients on anticoagulants. Recent studies support the safety of a more liberal approach for thoracentesis among patients with coagulopathy.

Methods: We conducted a survey to ascertain the practices of physicians regarding thoracentesis in patients with increased bleeding risk. The survey was administered to the email distribution lists of the American Association of Bronchology and Interventional Pulmonology and of the American Thoracic Society.

Results: The survey was completed by 256 attending physicians. Most were general pulmonologists practicing at academic medical centers. Most would perform a thoracentesis in patients receiving acetylsalicylic acid or prophylactic doses of unfractionated heparin or low molecular weight heparin (96%, 89% and 88%, respectively). Half of the respondents would perform a thoracentesis in patients on antiplatelet medications (clopidogrel and ticagrelor 51%; ticlopidine 53%). A minority would perform thoracentesis in patients on DOACs or infused thrombin inhibitors (19% and 12%, respectively). The only subgroup that had a higher proclivity for performing thoracentesis without holding medications were attending physicians practicing for under ten years. Relative to non-interventional pulmonologists, there were no significant differences in the responses of interventional pulmonologists.

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Erin M. DeBiasi and Jonathan T. Puchalski had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Erin M. DeBiasi, Terrence E. Murphy, Margaret A. Pisani, and Jonathan T. Puchalski contributed equally and substantially to the study design, data analysis and interpretation, and the writing of the manuscript.

Katy LB Araujo contributed with data analysis, figures and writing of the manuscript.

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Conclusion: There was variation in the practice patterns of attending physicians in performing thoracentesis in patients with elevated bleeding risk. Further data and guidelines regarding the safety of thoracentesis in these patients are needed.

Introduction

Among patients undergoing thoracentesis, post-procedural bleeding, including that from serious events such as hemothorax, has been observed historically 1-3% of the time.(1, 2) It is noteworthy that patients referred for thoracentesis often have comorbid conditions or take medications that potentially put them at higher risk of bleeding. One study of thoracentesis done on 312 patients found that 42% had one or more risk factors for bleeding.(3) In addition to warfarin and heparin products, there is also increasing use of direct oral anticoagulants (DOACs), resulting in a greater proportion of patients on anticoagulation. (4-7) There is no consensus regarding the management of anticoagulation and antiplatelet medications prior to low risk procedures such as thoracentesis(8-10) and to our knowledge, no recommendations specific to management of DOAC prior to thoracentesis. This survey sought to identify practice patterns of attending physicians who perform thoracentesis on patients with elevated bleeding risk due to either medication use or underlying coagulopathy.

Methods:

Survey Administration

From December 2017 to February 2018, we administered a thoracentesis practice pattern survey to the American Association for Bronchology and Interventional Pulmonology (AABIP) as well as the American Thoracic Society (ATS) Assemblies for Clinical Problems, Critical Care and Thoracic Oncology e-mail member distribution lists. Survey responses were only collected from self-identified attending physicians. Respondents were asked to only fill out the survey once if they received multiple times. A waiver of institutional review board approval was obtained through our academic institution. This voluntary and anonymous web-based survey was developed and disseminated using the survey platform Qualtrics (www.qualtrics.com) and was hosted by our academic institution.

Survey Design and Development

The survey addressed the attending physician practice patterns regarding performing thoracentesis on patients either with abnormal coagulation parameters or on medications that may increase bleeding risk (Supplement 1). The survey questions were developed by the interventional pulmonary research group at our academic institution which includes two attending interventional pulmonologists, one pulmonary and critical care attending and a statistician. Medications addressed in the survey were meant to represent classes of antiplatelet and anticoagulant medications commonly used in practice. Suggestions for duration of time that medications are held prior to performing procedures were largely based on reported elimination half-lives. Values of coagulation parameters such as INR and platelets were selected using commonly used thresholds as midpoints (platelets 50,000/ μ L and INR 2). It was piloted locally on selected attending and senior fellows in the Section of Pulmonary and Critical Care Medicine who routinely perform thoracentesis. A total number

of 12 physicians took the pilot survey and provided feedback. Feedback and suggestions were then used to modify the original survey.

The survey collected information on provider demographics and practice locations. Participants were then instructed to consider whether they would perform a thoracentesis on patients taking certain medications or with certain abnormal coagulation parameters. Participants were instructed to answer with the assumption that the thoracentesis was not urgent or life threatening and that the patient had no underlying renal or hepatic dysfunction. If participants would not perform a thoracentesis while a patient was actively taking the specified medication, they were given choices as to how to proceed. Please see Appendix 1 for full text of the distributed survey.

Statistical analysis

The responses to all questions were assessed and summarized as counts (%) within the categories available to respondents. The continuous variable age was classified into categories of ten year increments starting from 25 years through a final group of respondents 66 years and older. There was a total of 297 respondents, 256 of whom were attending physicians and therefore eligible to provide data. The non-attending respondents were fellow/resident (n=38), physician assistant/nurse practitioner (n=1), nurse (n=1), and respiratory therapist (n=1). From here on in this report the term respondents refers to attendings only. Bar plots of the percent of respondents who perform thoracentesis by minimum platelet count and maximal international normalized ratio (INR) were created. In like manner, bar plots were used to display the percentages of respondents who perform thoracentesis by class of anti-coagulant medication the patient was taking. Finally, odds ratios (95% credible intervals) representing attending physicians with 10 years or less procedural experience, relative to those with 10 or more years of corresponding experience, were plotted by class of anti-coagulant medication. The latter were generated with an unadjusted Bayesian logistic regression model where credible intervals that do not overlap with the null value of one were deemed statistically significant.

Results

Participant Characteristics

Table 1 summarizes the characteristics of the 256 surveys completed by attending physicians. Most respondents were male (80%) with the majority respondents between the ages 36-45 (45%, n=114) and with more than 11 years performing thoracentesis (51%, n=129). The majority of respondents practice in North America (83.9%, n=214) with a smaller number in Asia (8.2%, n=21), South America (2.6%, n=7), Europe (2.6%, n=7), Australia (1.8%, n=4) and Africa (0.8%, n=2). Most practice at a non-VA, academic center (71%, n=181). Most respondents were board certified/eligible and primarily practiced general pulmonary/pulmonary and critical care (64%, n=163), with a smaller number of respondents board certified/eligible and primarily practicing interventional pulmonary (29%, n=75). General pulmonary physicians were responsible for performing the majority of thoracentesis at most institutions (44%, n=112) with the remainder performed primarily by interventional pulmonary and interventional radiology (22%, n=56 and 25%, n=65, respectively). There

was variation in the number of thoracenteses each respondent performed and/or directly supervised on an annual basis with most reporting 6-25 thoracenteses per year (37%, n=95), although a similar number reported performing greater than 50 per year (33%, n=83). A strong majority routinely used ultrasound for thoracentesis (89%, n=228).

Coagulopathy

The bottom of Table 1 shows that few institutions had guidelines for performing thoracentesis in patients with either thrombocytopenia (20.3%, n=52) or elevated INR (22.7%, n=58). Figure 1A shows that most physicians (61%, n=153) would not perform a thoracentesis if platelets were below 50,000/ μ L. Fewer respondents had lower thresholds of 20,000/ μ L or 10,000/ μ L (24%, n=60; 6%, n=19, respectively). Less than one in 20 had a higher threshold of 100,000/ μ L (3.2%, n=8). Figure 1B demonstrates that most physicians' upper INR limit for not performing thoracentesis without correction or reversal was 1.5 (33%, n=82) or 2 (38%, n=96). Fewer respondents had limits above this, with only 18% (n=46) responding with an INR of 3, 3.6% (n=9) responding with an INR of 4, and 6.8% (n=17) responding with an INR of 5. If a patient's INR was above the physicians specified threshold, most would either hold medication (warfarin) and perform thoracentesis after INR reached their threshold (43%, n=108) or would transfuse FFP prior to thoracentesis (27%, n=67).

Unfractionated and low molecular weight heparin

Figure 2 displays the percentages of attendings who would perform thoracentesis by class of anti-coagulant medication the patient was taking. Most survey respondents would perform a thoracentesis on patients receiving either prophylactic doses of unfractionated heparin (UFH) or low molecular weight heparin (LMWH) (89%, n= 223 and 88%, n=216, respectively). Among respondents who delay a thoracentesis for patients on prophylactic UFH, the majority wait 6 hours after the last dose to perform the procedure. Among respondents who delay a thoracentesis for patients on prophylactic LMWH, the majority wait 7 hours since the last dose before performing the procedure.

A minority of respondents would perform a thoracentesis while patients were on either a therapeutic UFH drip or a therapeutic dose of LWMH (16%, n=41 and 26%, n=65 (Figure 2). More than half the respondents who delay thoracentesis for patients actively on UFH drip either hold the drip for 4 hours prior to procedure (52%, n=108) or wait 7-12 hours after last LMWH dose (58%, n=105) before performing the procedure.

Anti-platelet medications

Figure 2 also makes clear that nearly all respondents would perform a thoracentesis on a patient receiving acetylsalicylic acid (96%, n=236). About half of respondents would perform a thoracentesis on a patient on clopidogrel or ticagrelor (51%, n=125) or ticlopidine (53%, n=130). A smaller number would perform a thoracentesis on a patient on prasugrel (43%, n=105). If physicians elected to hold the medication prior to performing thoracentesis, most would hold each of the drugs 5-7 days (clopidogrel/ticagrelor 66%, prasugrel 50%, ticlopidine 54%).

Direct oral anticoagulants

Figure 2 further shows that a minority of respondents would perform a thoracentesis while a patient was on either an oral direct thrombin inhibitor (example: dabigatran) or an oral direct factor X-a inhibitor (e.g., rivaroxaban or apixaban, n=46 (19%) for each). Sixty-five percent of these respondents would hold the medication for 1-2 days prior to performing the procedure.

Infused thrombin inhibitors

Finally, Figure 2 also suggests that only a small minority of respondents would perform a thoracentesis on a patient taking an infused thrombin inhibitor (12%, n=30). Most preferred to hold the infusion for 4-6 hours before performing a thoracentesis (61%, n=213). The remainder would either hold the infusion 7-8 hours (31%, n=66) or consult with a pharmacist and/or review the elimination half-life of the drug (8%, n=16).

Subgroup analyses

Responses to questions regarding performance of thoracentesis while patients were receiving various classes of medications were further stratified based on respondent baseline characteristics including respondent sex, age, number of thoracentesis performed annually, number of years independently performing thoracentesis, and primary board certification. It was notable that there were no significant differences in practice patterns of physicians who identified as interventional pulmonologists (n=75) relative to all other physicians (N=181) across all classes of medication.

The only significant practice pattern differences noted were between attending physicians who had been practicing under 10 years versus those in practice greater than 10 years. Figure 3 shows that the former are more likely to perform thoracentesis on seven out of the eleven medication classes examined. This suggests that practitioners with less than 10 years of experience may be less conservative regarding the performance of thoracentesis among patients taking a broad array of anticoagulation medications.

Discussion

Thoracentesis is a commonly performed procedure with at least 173,000 performed annually in the United States. (11) The most common indications for thoracentesis are in patients with pleural effusions due to underlying cardiac disease or malignancy. These two groups of patients commonly use some form of anticoagulation or antiplatelet medications due to their inherent risk of thrombotic events. Temporary cessation of anticoagulation or antiplatelet medications is not without risk.

Post-procedural bleeding risk, including that from hemothorax, has been historically observed in 1-3% of patients undergoing thoracentesis.(1, 2) A recent study of a large cohort of patients indicate that the risk of significant bleeding from thoracentesis may be markedly less than previously observed.(12) A study of 9,320 patients undergoing thoracentesis reported an incidence of bleeding of only 0.18%. Given this low incidence rate,

thoracentesis is considered a “low risk” procedure with regard to bleeding complications. (13)

The majority of survey respondents indicated that for a non-emergent thoracentesis they would prefer holding any therapeutic anticoagulation including UFH, LMWH, oral or infused thrombin inhibitors or oral factor X-a inhibitors before commencing thoracentesis. Similarly, most would prefer INR within a subtherapeutic range (< 2) and platelets $> 50,000/\mu\text{L}$. Just under half of respondents would similarly hold antiplatelet medications (other than aspirin) prior to performing thoracentesis, a practice pattern likely based on historical recommendations. (1, 2, 14)

However, since the latter published guidelines there have been several studies that have established the level of safety for performing thoracentesis in patients on some of these medications or with abnormal coagulation parameters. (3, 12, 15-18) These studies have small enrollment numbers, were performed at single centers, and were either retrospective or observational by design. Several had mixed inpatient and outpatient populations and did not include a rigorous follow up protocol which may have led to uncaptured bleeding events. However these data, which come from four separate institutions, found no hemorrhagic complications in 572 patients with platelets $< 50,000/\mu\text{L}$ or in 3053 patients with INR > 1.49 . Similar data exists regarding safety of performing thoracentesis in patients on clopidogrel. Across three studies at three institutions, there was one bleeding complication that was managed with chest tube and blood transfusion from a total of 77 patients on clopidogrel. (3, 17, 18)

Since their introduction in 2010, the use of direct oral anti-coagulants (DOACs) has become increasingly popular. Although initially indicated only for prevention of cerebrovascular accidents in non-valvular atrial fibrillation, DOACs have an increasing number of indications including treatment of venous thromboembolism in patients with malignancy. (19) Primarily driven by an increase in DOAC prescriptions and a continuing decrease in use of warfarin, rates of anticoagulation for non-valvular atrial fibrillation have increased significantly this decade. (4-7) In Medicare patients in the United States, the number of claims for oral anticoagulation was 24.4 million in 2015. In that year, DOACs comprised 31% of all anticoagulation claims, which was a 127% increase compared to 2013. Warfarin claims decreased 8% over the time same time period. (6)

Given a relative dearth of evidence, guidelines regarding the perioperative management of DOACs have been based on expert consensus. (9) Despite the robust increase in their use in the past 5 years, there have been no studies regarding DOAC management with regards to thoracentesis. The most recent guidelines from the American College of Cardiology (ACC) recommend that for low risk procedures DOACs can be held 24-48 hours prior to the procedure contingent on creatinine clearance. However, they report that low risk procedures are “arguably best performed with no or limited interruption but experience with this approach using DOACs is limited.” Conversely, in regard to interruption of vitamin K antagonists, the ACC recommends not holding the medication for low risk procedures in the absence of other patient related risk factors for bleeding.

Since the aforementioned publication from ACC, a large meta-analysis from phase III trials involving DOACs and warfarin examined the periprocedural outcomes of patients who either had anticoagulation continued or withheld.(20) A total of 24,024 procedures were done on 19,353 patients. More than half of these procedures were endoscopic, dental, electrophysiological, or abdominal/thoracic/orthopedic surgery. The risk of major bleeding was no different between interrupted or noninterrupted strategies among patients using DOACs (2% versus 2.1%, respectively). There was a statistically significant 38% lower risk of periprocedural bleeding in a patient on a DOAC versus warfarin when anticoagulation was not withheld prior to surgery. If anticoagulation was withheld, there was a significantly lower risk of major bleeding if it was stopped on the same day of the procedure rather than a day prior. These data may indicate that for low risk procedures that continuation of DOAC therapy is safe.

Despite a consensus that thoracentesis is a low risk procedure for bleeding, recommendations from different societies or expert consensus panels vary with regard to periprocedural management of patients on anticoagulation or antiplatelet medications. This variability likely contributes to the practice pattern variation seen in this survey.(8-10). Overall, respondents were consistently conservative regarding management of anticoagulation or antiplatelet medications prior to thoracentesis. The survey did not capture any reasoning that influenced a respondent's answers. It is plausible that prior negative outcomes with bleeding complications had significant implications on current practice. Additionally, one can hypothesize that interventional pulmonologists or physicians that perform a greater number of thoracentesis annually may be more likely to perform thoracentesis without medication interruption/reversal or blood product transfusion; however, this was not seen in this cohort of survey respondents. The only significant difference in survey responses were observed between attendings performing thoracentesis for under 10 years versus those performing thoracentesis for greater than 10 years with the former more apt to perform thoracentesis in patients on uninterrupted anticoagulation or antiplatelet medications.

Strengths of this study include a variety of groups of respondents across geographic regions, age ranges and experience ranges. While this resulted in a modest sample size (N=256), it did provide detailed information across an array of classes of anticoagulant medications. We believe this is the most comprehensive set of data specifically designed to describe and quantify the practice patterns of physicians who perform thoracentesis on patients taking anticoagulant medication. The results of the study clearly support the need for larger, more comprehensive and inclusive studies to get a clear understanding of these practice patterns. There are several limitations of this study. First, it was administered in English in a web-based format to those on either the ATS or the AABIP e-mail membership lists. Respondents were therefore mainly from North America and most practiced in academic medical centers. We also do not have knowledge of the completion rate of the survey due to potential overlap of these groups, although presumably given the number of responses, the response rate is likely low. A reason for this is the inherent voluntary selection bias of survey respondents which may therefore not be truly representative of the population. Survey results also lack representation from community based physicians as well as interventional radiology (IR) groups. Survey respondents indicated that IR accounts for 25% of thoracentesis performed

at their institutions. Finally, although instructed to assume that thoracentesis was neither urgent nor life threatening and that patients had no other confounding medical comorbidities that may increase bleeding risk, thoracentesis is often an indispensable procedure. Respondent's answers may have been varied from their actual clinical practice when faced with a real patient scenario.

Conclusions

Rather than extrapolating recommendations from guidelines for a wide variety of other procedures with low risk for bleeding, large, prospective, multicenter studies specific to the management of anticoagulation and antiplatelet medications prior to thoracentesis are needed. This is especially important for DOACs as there are no current studies evaluating the safety of their continuation use prior to thoracentesis and because their use is so rapidly increasing. Prior literature specific to thoracentesis is typically based on low sample sizes from single institutions from studies that were performed retrospectively or without rigorous follow up protocols. While previous studies suggest that performance of thoracentesis in this population is safe, they are not sufficiently rigorous to inform official practice guidelines. Data from larger studies is needed to guide those providers who perform thoracentesis and to foster consistent patterns of periprocedural practice.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1:

A) Minimum platelet count that attending physicians would perform thoracentesis without transfusion. Physicians that chose lower values would also perform at all values higher than their chosen value. B) Upper INR threshold that attending physicians would not perform thoracentesis without correction, transfusion or delay

Figure 2:
Percentage of attending physicians who would perform a thoracentesis while patient is actively receiving class of medication

Figure 3: Odds ratios with credible intervals of the likelihood of performing thoracentesis in a patient actively on a class of medication of attending physicians with under 10 years of experience relative to those with greater than 10 years of experience.

Table 1.

Characteristics of Attending Physician Respondents

Characteristics of Participants and their Institutions	N=256
Participants	
Age in years, n (%)	
25 to 35	26 (10.2)
36 to 45	114 (44.5)
46 to 55	54 (21.1)
56 to 65	41 (16.0)
66 or older	19 (7.4)
Female, n (%)	52 (20.3)
Years of Performing Thoracentesis, n (%)	
0 to 5	73 (28.5)
6 to 10	52 (20.3)
11 to 15	30 (11.7)
15 or more	99 (38.7)
Use Ultrasound for Thoracentesis, n (%)	227 (88.7)
Number of Thoracentesis per Year, n (%)	
0 to 5	20 (7.8)
6 to 25	95 (37.1)
26 to 50	56 (21.9)
50 or more	83 (32.4)
Board Certified in Interventional Pulmonology, n (%)	75 (29.3)
Participant Institutions	
Primary Institution is non-VA Academic, n (%)	181 (70.7)
Institutional guidelines for thoracentesis in patients with thrombocytopenia, n (%)	52 (20.3)
Institutional guidelines for thoracentesis in patients with elevated INR, n (%)	58 (22.7)

Abbreviation: VA = Veteran's Administration, INR = international normalized ratio